REMARKS

Applicants respectfully request entry of the remarks submitted herein. Claim 1 has been amended herein for clarification purposes. Claims 1, 2, and 4-6 are currently pending. Reconsideration of the pending application is respectfully requested.

The 35 U.S.C. §112 Rejections

Claims 1, 2, and 4-6 stand rejected under 35 U.S.C. §112, first paragraph, as the Examiner asserted that those claims fail to comply with the written description requirement. The Examiner asserted that the skilled artisan cannot envision the detailed chemical structure of the genus of aquaporin-4 polypeptides. The Examiner further asserted that Applicants have only described the human aquaporin-4 polypeptide encoded by the DNA of SEQ ID NO:1 and that the specification does not provide adequate written description for polypeptides encoded by a polynucleotide that deviates from SEQ ID NO:1. The Examiner asserted that the claims do not require that the polypeptides of the present invention posses any particular distinguishing feature, and that Applicants are claiming a genus of polypeptides that are defined only by sequence similarity. This rejection is respectfully traversed.

In the current Office Action, the Examiner stated that "conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation" and cited the *Fiers v. Revel* case (25 USPQ2d 1601, 1606 (CAFC 1993)) and the *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* case (18 USPQ2d 1016). Applicants respectfully refer the Examiner to *Capon et al. v. Eshhar et al. v. Dudas* (418 F.3d 1349, 76 USPQ2d 1078 (Fed. Circ. 2005)) and *Invitrogen Corp. v. Clontech Laboratories, Inc.* (429 F.3d 1052 (Fed. Circ. 2005)). In *Invitrogen*, the Federal Circuit determined that the patent-in-suit contained an adequate written description of the claimed genus because the specification disclosed the sequence of a representative embodiment, demonstrated that that sequence encoded a polypeptide having the claimed features, and pointed to the availability of related sequences (related by both sequence homology and function) in the prior art. Both *Capon* and *Invitrogen* stand for the proposition that the amount of written description necessary to support generic claims "depends on a variety of factors, such as the existing knowledge in the particular field, the

extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter." *Capon et al. v. Eshhar et al. v. Dudas* (418 F.3d 1349, 1359 (Fed. Cir. 2005)). Neither *Capon* nor *Invitrogen* are inconsistent with the earlier *Fiers* and *Amgen* cases cited by the Examiner.

Applicants have identified the NMO antigenic polypeptide to which the NMO-autoantibody binds as aquaporin-4, and the claims explicitly require that an aquaporin-4 polypeptide or a fragment thereof used in the claimed methods is a polypeptide for which a NMO-specific autoantibody has specific binding affinity. The specification provides a significant amount of written description regarding NMO-specific autoantibodies and the NMO antigenic polypeptide, aquaporin-4. See, for example, the last paragraph on page 3 through line 2 of page 6, the last paragraph on page 14, and the third paragraph on page 19. In addition to describing the actual sequence of a representative aquaporin-4 (SEQ ID NO:1), the specification describes an aquaporin-4 polypeptide functionally (see, for example, the paragraph bridging pages 14 and 15) and provides numerous GenBank Accession Numbers of aquaporin-4 nucleic acids and polypeptides known in the art (see, for example, page 15).

In addition, the specification provides an adequate written description of fragments and variants (see, for example, pages 15-17). The specification contains disclosure regarding how to identify polypeptides that bind a NMO-specific autoantibody (see, for example, the paragraph bridging pages 5 and 6, the last two paragraphs on page 7, the sentence bridging pages 19 and 20, and Examples 3 and 6) as well as disclosure regarding specific binding affinity (see, for example, the last paragraph on page 6). Based on the maturity of the science and the predictability of the aspects at issue, Applicants have met the written description requirement for the claimed aquaporin-4 polypeptides and fragments thereof.

Contrary to the Examiner's assertions, the claimed genus of polypeptides is <u>not</u> solely defined by sequence similarity and the claims <u>do</u> require that the genus of polypeptides possesses a distinguishing feature (i.e., binding to an autoantibody). In view of the remarks herein, Applicants respectfully request that the rejection of claims 1, 2, and 4-6 under 35 U.S.C. §112, first paragraph, be withdrawn.

Claims 1, 2, and 4-6 stand rejected under 35 U.S.C. §112, first paragraph, as the Examiner asserted that the specification does not enable a skilled person to make or use the invention commensurate in scope with those claims. The Examiner asserted that while being enabling for using human aquaporin-4 polypeptides encoded by a nucleic acid of nucleotide sequence set forth in SEQ ID NO:1, the specification does not provide enablement for aquaporin-4 polypeptides that are variants to the corresponding wild-type molecules. The Examiner also asserted that there are no working examples in the specification of an aquaporin-4 polypeptide having less than 100% identity to the wild-type molecule encoded by the nucleic acid set forth in SEQ ID NO:1, and that the specification provides no guidance as to which amino acids might comprise the minimum residues of a fragment that retains the enabled functional property. The Examiner asserted that the claims encompass an unreasonable number of inoperative polypeptides. This rejection is respectfully traversed.

The claims are not directed toward any "NMO antigenic polypeptide or fragment thereof" but are limited to fragments "for which a NMO-specific autoantibody has specific binding affinity." Applicants respectfully refer the Examiner to *Hybritech Inc. v. Monoclonal Antibodies, Inc.* (802 F.2d 1367, 231 USPQ 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987)), which indicates that enablement "is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly extensive."

It is routine for those of skill in this art to generate fragments from a larger or full-length polypeptide and to determine whether or not those fragments bind to an antibody. In this case, the antibody is an autoantibody. That distinction, however, does not affect the routine approaches involved in screening fragments for antibody binding and, therefore, does not change the amount of disclosure that is required to enable the pending claims. In addition, not only are fragments enabled but variants or fragments that vary in sequence from SEQ ID NO:1 are enabled for the same reasons. That is, generating and determining the antibody binding capability of such variants is routine in the art. Using currently available equipment and procedures, many of which are automated, hundreds or thousands of different polypeptides (e.g., fragments and/or variants) can be readily and rapidly screened for specific binding affinity to a NMO-specific autoantibody without undue experimentation. Applicants' disclosure fully enables the pending claims.

On page 7 of the current Office Action, the Examiner stated that "one would reasonably expect that fragmentation of the aquaporin-4 polypeptide would abolish this desired activity because the minimum number of amino acids required for binding activity is at least 6 amino acids." Applicants are unclear as to the relevancy of this statement. The "desired activity" of the aquaporin-4 in the claimed method is to bind to and thereby detect the presence of the NMO-specific autoantibody. In fact, the Examiner's statement simply reinforces the fact that a person of ordinary skill in the art readily could carry out the requisite experiments and would know, for example, that polypeptides of less than 6 amino acids might not be optimal candidates for testing. In addition, the Examiner pointed to Harlow et al., which purportedly teaches that peptides of six residues in length will consistently elicit antibodies that bind to the original protein. Applicants submit that the elicitation of antibodies as taught by Harlow et al. also is not relevant to the claimed method of detecting the presence or absence of a NMO-specific autoantibody in a biological sample through binding of an aquaporin-4 polypeptide or fragment thereof to a NMO-specific autoantibody.

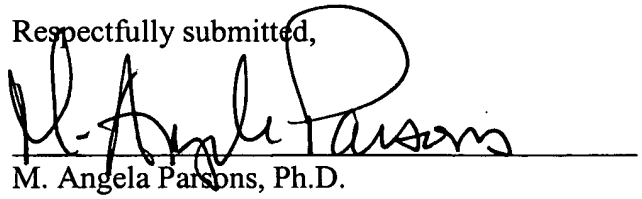
In view of the remarks herein, Applicants respectfully request that the rejection of claims 1, 2, and 4-6 under 35 U.S.C. §112, first paragraph, be withdrawn.

CONCLUSION

Please apply any charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: March 6, 2006



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